Patient Selection for Protected Percutaneous Coronary Intervention
Who Benefits the Most?

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KEYWORDS

• High-risk-PCI • Protected PCI • MCS devices • IABP • pLVAD • LAAD • VA-ECMO

KEY POINTS

- Definition of protected percutaneous coronary intervention (PCI) and hemodynamic impact of diverse mechanical circulatory support devices.
- Clinical criteria for patient selection for protected PCI.
- Procedure-related criteria for patient selection for protected PCI.
- Algorithm and scoring system for patient selection for protected PCI.

INTRODUCTION

A development of percutaneous coronary intervention (PCI) with device innovation, novel skills, and effective antiproliferative medications allows for addressing increasingly complex coronary artery disease (CAD).[1] However, simultaneously, patients are presenting nowadays with higher rates of comorbidities and more complex CAD, which may lead to a lower physiologic tolerance for complex PCI. This patient group would be poor candidates for coronary artery bypass grafting (CABG) because of the high risk of surgical morbidity and mortality.[2]

As an alternative approach, the concept of so-called "protected PCI" has been developed, in which mechanical circulatory support (MCS) is used for the PCI in this high-risk patient group. The purpose of MCS is to provide hemodynamic support for complex PCI, and concurrently to reduce left ventricular systolic work and myocardial oxygen demand while maintaining systemic and coronary perfusion.[3] Currently, the following devices are available for MCS: intra-aortic balloon pump (IABP), percutaneous left ventricular assist devices (pLVAD), left atrial to aorta assist devices (LAAD), and veno-arterial extracorporeal membrane oxygenation (VA-ECMO). Using MCS devices in combination with an optimal selection of patients and devices would potentially improve the success rate of interventional procedures and clinical outcomes in these high-risk patients.[4,5]

However, since multiple treatment modalities are available and the precise definition of "high-risk patients" has not yet been established, it is still not clearly determined who benefits the most from protected PCI and which MCS device offers the best result in each clinical scenario. Hence, this review aims to provide practical approaches for the appropriate selection of patients and MCS device types by outlining current clinical data that assess utility of diverse MCS devices in high-risk patients undergoing protected PCI.

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DEFINITION OF PROTECTED PERCUTANEOUS CORONARY INTERVENTION

The evolution of PCI techniques has enhanced the number of patients eligible for PCI of complex coronary lesions, for example, unprotected left main coronary stenosis, heavily calcified stenosis, and chronic total occlusion.[6] Nevertheless, each aspect of PCI, beginning from guide catheter engagement and ending with balloon inflation and stent deployment, is associated with potential risk of vascular damage and impairment of myocardial perfusion. Especially, patients with more complex CAD evaluated by higher SYNTAX (Synergy between Percutaneous Coronary Intervention with Taxus and Cardiac Surgery) score and concurrent higher surgical mortality assessed by higher STS (the Society of Thoracic Surgeons) score would not be suitable for either PCI[7] or for CABG.[8] Specifically, the PCI in patients with reduced coronary perfusion gradients between coronary arterioles and venules could cause a severe myocardial ischemia and consequently ischemia-triggered cardiac arrhythmias or further depression of an already impaired left ventricular ejection fraction (LVEF), leading to circulatory collapse and cardiac arrest.[9,10] Furthermore, complete or sufficient revascularization could not be guaranteed due to hemodynamic instability during the procedures. To avoid this fatal consequence, so-called protected PCI using MCS device as an alternative strategy for safely achieving complete revascularization has been used for more than 25 years.[11] The purpose of MCS is to decrease myocardial oxygen demand by reducing left ventricular volume (preload) and pressure (afterload) during high-risk PCI.[12] Another goal of MCS is to achieve sufficient cardiac output to maintain myocardial, cerebral, renal, mesenteric, and peripheral tissue perfusion, thereby preventing systemic shock syndrome. In addition, the use of appropriate MCS devices can provide sufficient time to safely perform high-risk PCI with optimal results in this patient group who would not otherwise tolerate complete revascularization.[13]

HEMODYNAMIC IMPACT OF MECHANICAL CIRCULATORY SUPPORT DEVICES

Currently, diverse types of percutaneous MCS with different characteristics and hemodynamic impact are available for high-risk PCI.[14] First, IABP supports hemodynamic circulation by inflating and deflating the balloon based on an electrocardiogram (ECG) or pressure triggers.[15] The balloon inflating occurs with the onset of diastole timed to the middle of the T-wave on ECG. Thereafter, the balloon deflates rapidly at the beginning of left ventricular systole corresponding to the pear of the R-wave on ECG. The IABP decreases myocardial oxygen demand by reducing left ventricular afterload, and increases coronary artery perfusion by enhancing diastolic blood pressure. However, there are some functional limitations of IABP. Whereas mean arterial pressure and coronary blood flow are increased by using IABP, it offers only modest left ventricular unloading defined by reducing left ventricular volume and pressure (**Fig. 1**A). A stable electrical rhythm is also a prerequisite for the optimal hemodynamic effect from IABP, because IABP works depending on the surface ECG. The further limitations of IABP are dependence on native left ventricular function, balloon capacity, and accurate timing of balloon inflation and deflation.[16]

Second, the pLVAD is a continuous nonpulsatile microaxial screw pump deployed into the left ventricle across the aortic valve to pump blood from the left ventricle to the ascending aorta.[17] In this way, the pLVAD increases forward flow to the ascending aorta and mean arterial pressure. At the same time, it reduces myocardial oxygen demand and pulmonary capillary wedge pressure.[18] In contrast to IABP, the hemodynamic support from pLVAD is dependent neither on the native left ventricular function of patients nor on electrical stability due to its direct continuous propelling of blood from the left ventricle to the ascending aorta. The pLVAD leads to a remarkable unloading of the left ventricle by reducing left ventricular systolic and diastolic pressures, left ventricular volumes, and stroke volume (**Fig. 1**B). In case of biventricular failure or unstable ventricular arrhythmias, concomitantly using a right ventricular assist device should be considered to maintain left ventricular preload and optimal hemodynamic support from pLVAD.

The LAAD is one of the MCS devices that extracorporeally pumps blood from the left atrium via a transseptally placed left atrial cannula to the iliofemoral arterial system, thereby bypassing the left ventricle.[17] The bypass of blood from the left atrium induces indirectly optimal left ventricular unload at a similar level to pLVAD that enables direct unloading of the left ventricle (see **Fig. 1**B). By this means, the LAAD reduces wall stress and myocardial oxygen demand.[19] However, the need for a transseptal puncture is an important obstacle for clinical use of LAAD.

Finally, VA-ECMO provides both oxygenation and circulation. A venous cannula drains deoxygenated blood into a membrane oxygenator for gas exchange, and oxygenated blood is subsequently infused into the patient via an arterial

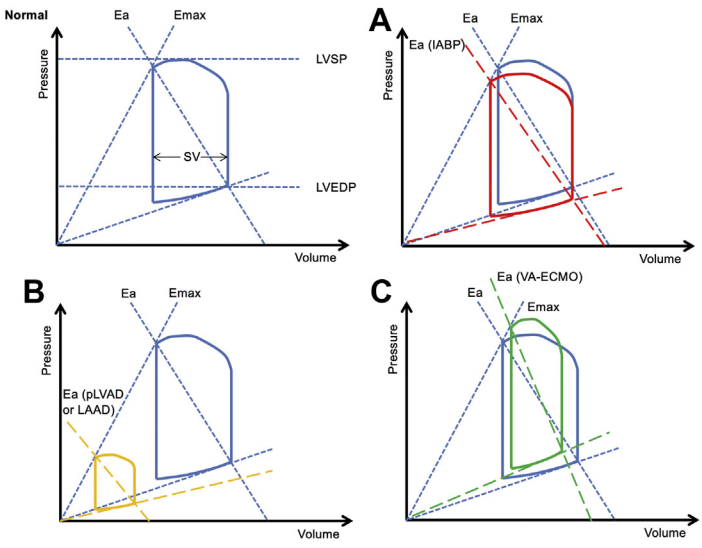

Fig. 1. Hemodynamic imbalance in acute myocardial infarction and cardiogenic shock, and hemodynamic impact of various MCS devices are illustrated by the pressure-volume loop. The normal pressure-volume loop is shown in blue. Emax representing a load-independent left ventricular contractility is defined as the maximal slope of the end-systolic pressure-volume point under various loading conditions, known as the end-systolic pressure-volume relationship. Effective arterial elastance (Ea) is a component of left ventricular afterload and is defined as the ratio of left ventricular systolic pressure (LVSP) and stroke volume (SV). (*A*) Pressure-volume loop in using IABP demonstrates a mildly decreased left ventricular end-diastolic pressure (LVEDP) and LVSP, leading to decreased an Ea. (*B*) Pressure-volume loop with pLVAD and LAAD shows a substantially decreased LVEDP, LVSP, and SV. The net effect is a pronounced reduction of left ventricular preload and afterload. (*C*) Pressure-volume loop with VA-ECMO without left ventricular venting indicates a decreased SV, whereas LVEDP und LVSP are significantly increased with a net effect of substantial increase of left ventricular afterload. (*Adapted from* Rihal CS, Naidu SS, Givertz MM, et al. 2015 SCAI/ACC/HFSA/STS Clinical Expert Consensus Statement on the Use of Percutaneous Mechanical Circulatory Support Devices in Cardiovascular Care: Endorsed by the American Heart Assocation, the Cardiological Society of India, and Sociedad Latino Americana de Cardiologia Intervencion; Affirmation of Value by the Canadian Association of Interventional Cardiology-Association Canadienne de Cardiologie d'intervention. J Am Coll Cardiol. 2015;65(19): e7-e26.)

cannula. VA-ECMO provides systemic circulatory support with flows sometimes exceeding 6 L/min depending on cannula sizes. However, it can significantly increase afterload on the left ventricle (Fig. 1C), thereby potentially reducing left ventricular stroke volume, increasing myocardial oxygen demand, and necessitating "venting" of the left ventricle by concomitant IABP or pLVAD.[20,21] In contrast to conventional VA-ECMO, the novel pulsatile ECMO triggered by ECG provides a more sufficient coronary perfusion with less increase in afterload.

CLINICAL CRITERIA FOR PATIENT SELECTION FOR PROTECTED PERCUTANEOUS CORONARY INTERVENTION

Recently, the clinical practice guidelines recommend consideration of the use of these devices in the setting of high-risk PCI.[3] To avoid underutilization or overutilization of MCS devices during high-risk PCI and to minimize the associated risk, however, a proper patient selection is paramount. Based on patient inclusion criteria adopted in prior various studies assessing utility of protected PCI, the following factors are generally considered as major criteria in patient selection for protected PCI[22] (Table 1). First, one of these factors is the lesion characteristic that determines the complexity of PCI reflecting the technical perspectives and the potential risk of complications. It includes unprotected left main coronary stenosis, distal left main bifurcation stenosis, multivessel disease with high SYNTAX score (≥33), myocardial jeopardy score (≥8/12), last remaining coronary conduit, heavily calcified lesions (type C lesion), and chronic total occlusions. Shamekhi and colleagues[23] revealed that patients undergoing protected PCI with pLVAD achieved more often a complete revascularization without the occurrence of cardiac death at 30 days of follow-up compared with patients undergoing unprotected PCI despite a higher SYNTAX score (45% vs 36%, $P = .07$) and more often complex left main bifurcation lesions (71% vs 29%). Moreover, a similar major adverse cardiac event rate (MACE) at 1 year of follow-up between both groups was shown despite severe basic characteristics of the protected PCI group. These are consistent with results of another study, in which patients undergoing protected PCI with pLVAD had also a decreased rate of residual stenosis and increased rate of procedural success compared with patients with unprotected PCI. The short-term and

Table 1
Clinical criteria for patient selection for protected PCI

Lesion characteristic	Unprotected left main coronary stenosis Distal left main bifurcation stenosis Multivessel disease with higher SYNTAX score (≥33) or myocardial jeopardy (≥8/12) Last remaining coronary conduit Heavily calcified lesions (type C lesion) Chronic total occlusions
Severe decompensated heart failure	LVEF (≤30–40%) NYHA classification III-IV Killip classification II-IV Electrical instability (eg, ventricular tachycardia)
Patient comorbidities with higher STS-score or EuroSCORE	Increased age (>75 y) Chronic obstructive lung disease Chronic kidney disease Peripheral vascular disease Diabetes mellitus
Hemodynamic parameters	Cardiac index (<2.2 L/min per m^2) Pulmonary capillary wedge pressure (>15 mm Hg) Mean pulmonary artery pressure (>30 mm Hg)

Abbreviations: LVEF, left ventricular ejection fraction; NYHA, New York Heart Association; PCI, percutaneous coronary intervention; STS, Society of Thoracic Surgeons; SYNTAX, synergy between percutaneous coronary intervention with taxus and cardiac surgery.

long-term outcomes in terms of MACE were also similar despite the significantly higher SYNTAX score in the protected PCI group (33% vs 24%, $P<.01$).[24] The extended randomized BCIS-1 trial (Balloon Pump-Assisted Coronary Intervention Study) demonstrated that protected PCI using IABP reduced relatively a long-term all-cause mortality in patients with higher myocardial jeopardy score (≥8) compared with the unprotected PCI group.[25]

Second, protected PCI might be proper for patients with severe decompensated heart failure with reduced LVEF (≤30–40%), New York Heart Association (NYHA) classification III-IV, Killip classification II–IV, or electrical instability (eg, ventricular tachycardia). Ameloot and colleagues[5] showed that patients with severely reduced LVEF (median 24%) and concomitant higher SYNTAX score (median 33) have benefited from protected PCI using pLVAD in terms of survival rate. In a registry trial involving patients with decreased LVEF (mean 31%) and higher SYNTAX score (median 37), it was shown that protected PCI with pLVAD significantly improved LVEF and NYHA class of these high-risk patients.[26] In the PROTECT II trial (Prospective Randomized Clinical Trial of Hemodynamic Support with Impella 2.5 vs Intra-Aortic Balloon Pump in Patients undergoing High-Risk Percutaneous Coronary Intervention) involving patients with reduced LVEF (<30%–35%) and concurrent unprotected left main stenosis or 3-vessel disease, patients undergoing protected PCI with pLVAD have achieved a more hemodynamic stabilization.[27] Thereby, the frequent occurrence of complete revascularization and the associated reduction of MACE in the protected PCI group might be explained.

Third, patient comorbidities, including increased age (>75 years), chronic obstructive lung disease, chronic kidney disease, peripheral arterial disease, and diabetes mellitus, should be evaluated by STS-score or EuroSCORE when selecting patients for protected PCI. Patients with higher comorbidities assessed by higher STS-score or EuroSCORE could not be suitable for surgical revascularization due to the underlying increased expected risk of mortality and morbidity,.[28–30] In a multicenter registry study, it was shown that protected PCI using pLVAD might be a safe and effective alternative approach to revascularize coronary lesions in patients with higher SYNTAX score (median 32) and concurrent higher logistic EuroSCORE (median 14.7).[31] Another study demonstrated also the safety of both pLVAD and LAAD for protected PCI, especially in patients with complex coronary anatomy and reduced LVEF (median 31%) who were rejected for CABG because of higher mortality risk (median STS-score of 4.2%).[32] Recently, Baumann and colleagues[33] demonstrated in a multicenter registry study that patients undergoing protected PCI with pLVAD due to both higher SYNTAX score (median 33) and higher

EuroSCORE II (median 7.2%) had acceptable clinical results at 180 days of follow-up regarding MACE (22%) and all-cause mortality (18%).

Finally, hemodynamic parameters are also regarded as key factors, especially reduced cardiac index (<2.2 L/min per m^2), increased pulmonary capillary wedge pressure (>15 mm Hg), and mean pulmonary artery pressure (>30 mm Hg). The safety and efficacy of IABP and LAAD for protected PCI could be demonstrated in a randomized study including patients with a cardiac index less than 2.1 L/min per m^2 indicating an onset of cardiogenic shock.[34] In contrast, however, no study could clearly demonstrate the mortality advantage of MCS devices in patients with already manifested severe cardiogenic shock despite improvement in hemodynamic and metabolic parameters by using MCS devices.[35–38]

PROCEDURE-RELATED CRITERIA FOR PATIENT SELECTION FOR PROTECTED PERCUTANEOUS CORONARY INTERVENTION

In addition to the previously mentioned clinical criteria, procedure-related factors also should be considered in patient selection for protected PCI to reduce procedure-related complications and thus to improve clinical outcomes (**Table 2**). These depend basically on the selection of MCS devices due to the different implantation techniques and operating mechanisms.[39] The factor that is independent of types of MCS devices is a pathologic peripheral vessel condition, such as tortuosity and/or peripheral arterial disease. This factor does not actually represent an absolute contraindication for the implantation of MCS devices of all types.[3] However, it is associated with increased risk of limb ischemia or mechanical malfunction of MCS devices.[40] Especially in patients with known peripheral arterial disease, severity of disease should be assessed by imaging diagnostics, such as duplex ultrasonography or even computed tomography angiography to determine the appropriate access vessel for insertion of the device's sheath. In this regard, for example, patients with severe peripheral arterial disease or tortuosity in iliofemoral vessels could benefit more from pLVAD with an axillary access than from the other devices.[22]

In addition, the indication of protected PCI should be carefully evaluated in patients with aortic valve disease (ie, aortic regurgitation or aortic stenosis).[41] Even with mild aortic regurgitation, all types of MCS devices could increase significantly the volume of regurgitation due to increased aortic pressure, leading to further dilatation of aorta and left ventricle and consequently severe decompensating hemodynamics.[42,43] Specifically, in case of pLVAD in patients with aortic regurgitation, an optimal forward flow mediated by pLVAD could be not guaranteed due to the lack of a competent valve separating between the left ventricle and aorta.[44] Moreover, patients with an aortic stenosis will be also poorly served by pLVAD because of difficult placement caused by the aortic stenosis and an increased risk of thromboembolism as well as rupture. Therefore, assessment of aortic valve using transthoracic (TTE) or transesophageal echocardiography (TEE) before protected PCI is recommended.

The presence of thrombus is also one of criteria that should be excluded by TTE or TEE before the planed protected PCI using particularly pLVAD or LAAD.[44] An ingestion of left ventricular clot in pLVAD commonly leads to shutdown of the device. The likelihood of clot ingestion resulting in embolization is extremely unlikely; however, a mobile thrombus represents a risk for systemic embolization with any left ventricular catheter placement. When using LAAD, thrombus in the left atrium could lead to the shutdown of the LAAD or/and a systemic embolization, such as an ischemic stroke, mesenteric ischemia, and renal infarction. Hence, preprocedural visualization of the left ventricle and atrium excluding the presence of thrombus is advisable.

In protected PCI with pLVAD, LAAD, or VA-ECMO, an adequate anticoagulation is indispensable to prevent thrombus formation that leads to malfunctions of devices and systemic thromboembolism.[45] In this context, patients with hemorrhagic diathesis, for example, thrombocytopenia, liver synthesis disorder, von Willebrand disease, or disseminated intravascular coagulation, might benefit rather from protected PCI using IABP instead of pLVAD, LAAD or VA-ECMO.

ALGORITHM AND SCORING SYSTEM FOR PATIENT SELECTION FOR PROTECTED PERCUTANEOUS CORONARY INTERVENTION

According to recommendations of European Society of Cardiology 2017, IABP insertion should be considered in patients with hemodynamic instability or cardiogenic shock due to mechanical complications (Class IIa), whereas no other devices are recommended.[46] In patients with acute myocardial infarction complicated by cardiogenic shock, short-term MCS may be considered regardless of device types (Class IIb). According to the guidelines of American College of Cardiology/American Heart Association/Society for Cardiovascular Angiography and Interventions, elective insertion of an appropriate MCS device

Table 2
Procedure-related criteria for selection of patients and MCS devices for protected PCI

Criterium		Available MCS Devices
Peripheral vessel condition assessed by duplex ultrasonography or CTA	Iliofemoral tortuosity Iliofemoral peripheral arterial disease	Axillary pLVAD, IABP
Aortic valve disease assessed by TTE or TEE	Aortic regurgitation Aortic stenosis	No devices recommended IABP, LAAD, VA-ECMO
Presence of thrombus assessed by TTE or TEE	Thrombus in left ventricle Thrombus in left atrium	IABP, LAAD, VA-ECMO IABP, VA-ECMO
Contraindication for anticoagulation	Thrombocytopenia Liver synthesis disorder von Willebrand disease Disseminated intravascular coagulation	IABP

Abbreviations: CTA, computed tomography angiography; IABP, intra-aortic balloon pump; LAAD, left atrial to aorta assist devices; MCS, mechanical circulatory support; PCI, percutaneous coronary intervention; pLVAD, percutaneous left ventricular assist devices; TEE, transesophageal echocardiography; TTE, transthoracic echocardiography; VA-ECMO, veno-arterial extracorporeal membrane oxygenation.

as an adjunct to PCI has been recommended in carefully selected high-risk patients who have a vessel subtending a large territory on a background of severely depressed left ventricular function, unprotected left main, or last remaining conduit (Class IIa).[47]

So far, however, no established algorithm or scoring system reflecting all clinical and procedure-related criteria has been developed that can be generally used in patient selection for protected PCI to prevent underestimating or overestimating. Werner and colleagues[48] suggested in their expert consensus an algorithm for patient selection for protected PCI based on coronary complexity, LVEF, cardiac index, and comorbidities; however, herewith also no procedure-related criteria were considered when selecting patients for protected PCI. In the algorithm suggested by Atkinson and colleagues,[22] an evaluation of femoral vessel was reflected to determine

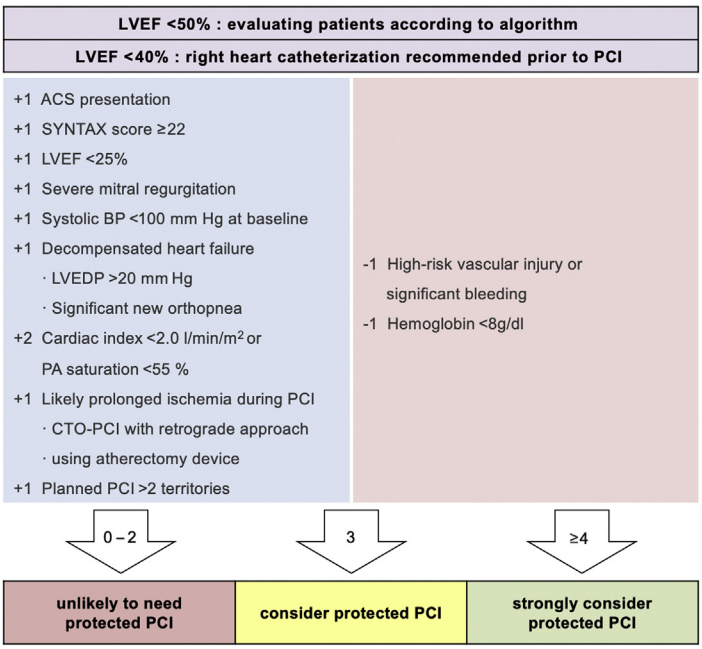

Fig. 2. Proposed scoring system based on clinical factors for optimal patient selection for protected PCI. ACS, acute coronary syndrome; BP, blood pressure; CI, cardiac index; CTO, chronic total occlusion; LVEDP, left ventricular end-diastolic pressure; PA, pulmonary artery. (*Adapted from* McCabe JM. Hemodynamic support for CTO PCI: who, when & how. Presented at Transcatheter Cardiovascular Therapeutics (TCT). September 21-25, 2018, San Diego, California.)

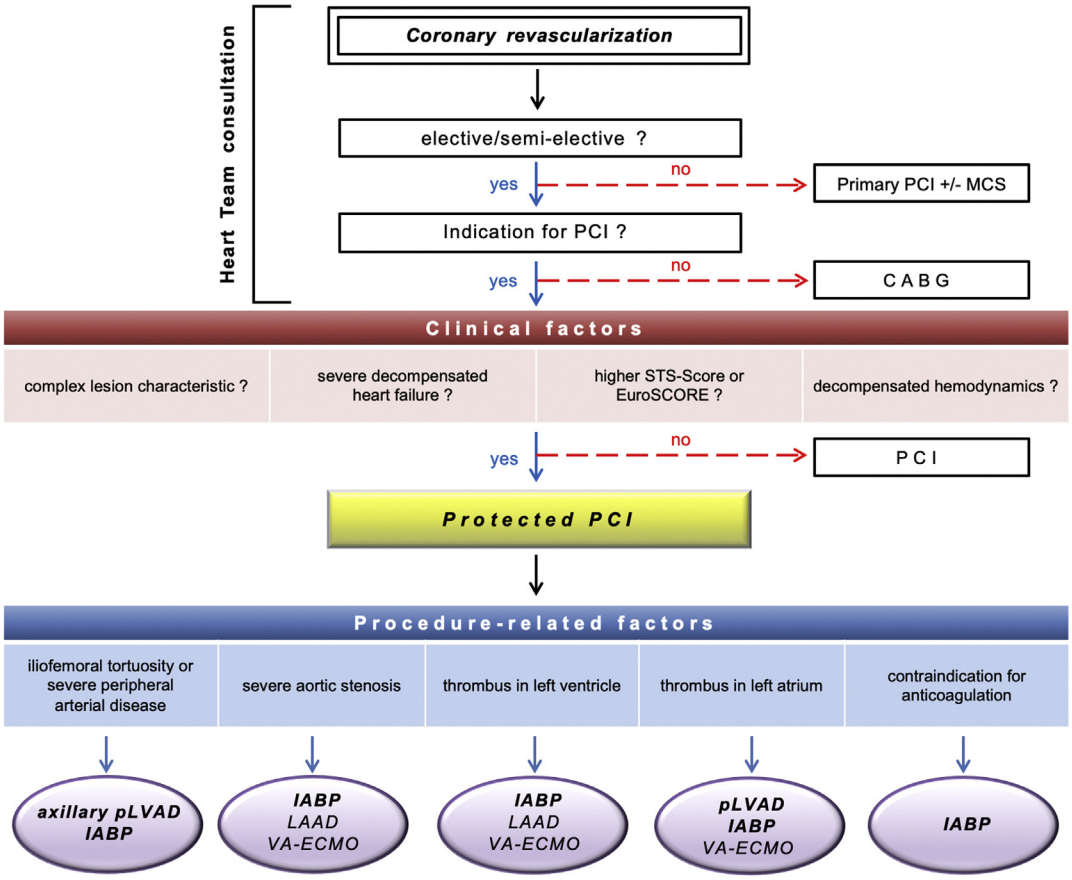

Fig. 3. Proposed practical approach for patient selection for protected PCI depending on the clinical and procedure-related factors. IABP or pLVAD should be preferred for protected PCI if there are no negative procedure-related factors for their use.

the access vessel for inserting MCS devices, but no other procedure-related factors were described in detail. A single-center registry by McCabe[49] evaluating a proposed scoring system to guide patient selection for protected PCI is ongoing, and findings regarding the adequacy of these characteristics to predict efficacy and safety of upfront protected PCI are still pending (Fig. 2). Based on the previously proposed algorithms, Fig. 3 suggests a practical approach for patient selection for protected PCI depending on the clinical and technical aspects. To improve efficacy and safety of protected PCI in these high-risk patients exhibiting higher mortality, further clinical studies should be conducted to develop a universal reliable algorithm to select appropriate patients for protected PCI.

SUMMARY

Protected PCI represents one of the most advanced PCI types using several MCS devices to maintain sufficient cardiac output and reduce myocardial oxygen demand in high-risk patients who would not otherwise tolerate complete revascularization of complex coronary lesions. However, a precise selection of patients for protected PCI based on various clinical criteria is imperative to achieve hemodynamic and prognostic benefit in this patient group with higher morbidity and mortality burden. Moreover, the use of MCS devices for protected PCI should be also strictly individualized based on procedure-related factors to prevent device-associated complications. Further registry and randomized trials should be conducted to establish an evidence-based algorithm and scoring system that enables more careful selection of patients for protected PCI to improve clinical outcomes.

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DISCLOSURE

The authors have nothing to disclose.

CONFLICT OF INTEREST

The authors declare that they have no potential conflict of interest.

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